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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,895	10/07/2002	Archibald Lovatt	CKFW-P01-003	1358

28120 7590 05/21/2007

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,895	LOVATT ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *31-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/13/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-30, filed February 27, 2007, is acknowledged. Applicant argues that the simultaneous examination of Groups I and II would present no significant additional burden for the examiner since they recite many similar elements and the searches would overlap significantly. In response to this argument, the Office notes that the instant application is a national stage entry of an international application and is subject to lack of unity practice. Since search burden is not a factor in the determination of lack of unity, Applicant's arguments are not found persuasive. Therefore, the restriction is deemed proper and made FINAL.

2. Claims 1-36 are pending. Claims 1-30 are under examination. Claims 31-36 are withdrawn from consideration being drawn to non-elected subject matter.

Claim Objections

3. Claims 1-30 are objected to for a minor informality: Claim 1 and all dependent claims recite a grammatical error in step a), "an oligonucleotide that is complementary to portion of the RNA template". The phrase should recite, "an oligonucleotide that is complementary to a portion of the RNA template". Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 24 recites, "said method includes a suppressor of reverse transcriptase activity of DNA polymerases". Dependent claims 25-28 recite more details regarding the suppressor. However, it is unclear where the suppressing action of the suppressor takes place in the method steps. Clear method steps are required in order for the metes and bounds of the claims to be discerned.
- Claim 29 recites, "wherein the concentration of activated calf thymus DNA", which lacks antecedent basis in claim 1 from which claim 29 depends.
- Claim 30 recites, "wherein activated calf thymus DNA is used to further reduce interference", however, it is unclear where this step takes place in the method steps. Clear method steps are required in order for the metes and bounds of the claims to be discerned.

Claims Summary and Interpretation

5. The claims are drawn to a method for detecting reverse transcriptase (RT) activity in a test sample. The steps are comprised of the following:

a) Contact the test sample with an RNA template and an oligonucleotide, wherein the RNA template and oligonucleotide anneal and a DNA strand is synthesized if RT is present in the test sample. Specifically, the RT activity is retroviral RT activity from a virus such as FeLV, HIV or porcine endogenous retrovirus (PoERV). The test sample is any variety of biological

tissue or body fluid. The RNA template is selected from Brome Mosaic virus (BMV), bacteriophage MS2 RNA and genomes of RNA viruses with no DNA intermediate. The RT reaction is carried out a pH of above 5.5 and below 8.5.

b) Subject the mixture in a) to a treatment that substantially inactivates any DNase present. The DNase inactivation step is accomplished by heat or a proteinase.

c) Amplify the synthesized DNA using a DNA polymerase, whereby the amplified DNA is detected by incorporation or release of a label. The step of amplification of the synthesized DNA is carried out under conditions where a probe possessing a reporter and suppressor molecule anneals to a strand of the template nucleic acid, and nuclease activity of the DNA polymerase cleaves the suppressor molecule or the reporter molecule from the probe, and the non-suppressed reported molecule is detected. The reporter molecule is a fluorescent molecule, such as FMA and/or TAMRA. Although it is not entirely clear where the suppressing activity of the reverse transcriptase activity takes place in the method, the suppressor of RT activity of DNA polymerases is activated DNA, such as activated calf thymus DNA (acT DNA).

d) Detect any amplified DNA by way of the incorporation or release of the label.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 5-16, 18-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Arnold *et al.* (*BioTechniques*, July 1998, 25(1):98-106, "Arnold"). The claims are summarized above. Arnold discloses a one-step fluorescent prove product-enhanced reverse transcriptase assay (abstract). Arnold discloses the modification of the already known RT-PCR method by utilizing the 5' nuclease activity of Taq DNA polymerase to digest a hybridization probe labeled with a FAM at the 5' end, and TAMRA near the 3' end (page 99, first column). The RNA template (0.3 micrograms of bacteriophage MS2, naturally free of telomerase target sequences) and an oligonucleotide probe are mixed and annealed (page 103, first column). The reaction mixture to which the virally-infected sample is added is at pH 8.3 (page 103, first column). The virally-infected samples include AMV, MuLV and SRV-1 (see Table 1). Arnold discloses that all samples were assayed in triplicate and that RT and cDNA amplification were performed using the following parameters: 42°C for 30 minutes for RT, 95°C for 10 minutes to activate the Taq DNA polymerase, followed by 35 or 40 cycles of denaturation followed by annealing and extension (page 103, first and second columns). Although Arnold does not teach that the 10 minute treatment at 95°C substantially inactivates and DNase present in the mixture, the treatment is expected to have exactly that effect since it is the same treatment used by Applicant.

With regard to the limitation in claim 8 about stimulating retrovirus production prior to assaying the sample, the claim does not specify how this step is performed. Thus, the production of retrovirus for the sample used in Arnold's assay qualifies as stimulating retrovirus production prior to assaying the sample. Therefore, the claims are anticipated by Arnold's assay.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as unpatentable over Arnold *et al.* (*BioTechniques*, July 1998, 25(1):98-106, "Arnold"), in view of Burke (*Promega Notes Magazine*, 1996, Number 58, page 43, computer print-out is three pages) and Palmiter *et al.* (U.S. Patent 5,583,009, "Palmiter"). The claims are summarized above, as are the teachings of Arnold. Arnold does not disclose the use of a proteinase to substantially inactivate any DNase present in the sample prior to amplification.

However, Burke discloses that in instances where DNase is present in the sample (if the treatment is necessary prior to amplification), its removal can be performed by a phenol extraction and subsequent precipitation, or by heating at 95°C for 10 minutes (second page of computer print-out, first complete question/answer). Although Burke does not teach the use of a proteinase to remove the DNase, it would have been obvious to use a proteinase, such as proteinase K. Palmiter discloses the use of proteinase K in an RT-PCR method following treatment of total nucleic acid with DNase (col. 15, second paragraph of Example 6).

One would have been motivated to use a DNase in order to purify the RNA sample as much as possible, and then inactivate the DNase prior to RT-PCR so that the results more accurately reflect the RT activity (Burke, first page of computer print-out, last question/answer). One would have had a reasonable expectation of success that further purification of the RNA in

the sample would yield more accurate results given that the DNA desired for amplification is the synthesized DNA and not DNA already present in the sample. Therefore, the claimed embodiments would have been obvious to one of ordinary skill in the art at the time the invention was made.

10. Claims 1-4 are rejected under 35 U.S.C. 103(a) as unpatentable over Arnold *et al.* (*BioTechniques*, July 1998, 25(1):98-106, "Arnold") in view of Martin *et al.* (*The Lancet*, 1998, 352:692-694, "Martin"). The claims are summarized above, as are the teachings of Arnold. Arnold's method is disclosed as generally applicable to retroviruses, but the specific viruses FeLV, HIV or PoERV (or PERV) are not named.

However, Martin discloses RT-PCR for RT activity of PoERV-infected HEK293 cells (page 694, first column, fourth full paragraph). It would have been obvious to use Arnold's assay for the detection of PoERV RT activity. One would have been motivated to detect RT activity of PoERV because PoERV often infects organs that are potentially used for xenotransplantation. The use of PoERV-infected organs for xenotransplantation is highly undesirable because of the unknown effects of PoERV in humans, for example (Martin, page 692, second column, "Introduction"). Therefore, one would have been motivated to use a highly sensitive RT-PCR assay to detect PoERV. One would have had a reasonable expectation of success that Arnold's method would have detected PoERV because Arnold teaches that the assay is generally applicable to retroviruses (abstract). Therefore, the claimed embodiments would have been obvious to one of ordinary skill in the art at the time the invention was made.

11. Claims 1 and 24-30 are rejected under 35 U.S.C. 103(a) as unpatentable over Arnold *et al.* (*BioTechniques*, July 1998, 25(1):98-106, "Arnold") in view of Lugert *et al.* (*BioTechniques*, 1996, 20:210-217, "Lugert"). The claims are summarized above as are the teachings of Arnold. Although Arnold acknowledges that DNA polymerases can exhibit RT activity (page 105, first column), Arnold does not disclose the use a calf-thymus DNA to suppress RT activity of DNA polymerases.

However, Lugert discloses that DNA polymerases' RT-like activity can be suppressed by including increasing amounts of activated DNA, specifically calf thymus DNA, in the RT reactions (abstract and page 210-211, bridging paragraph). It would have been obvious to use Lugert's step of suppressing RT activity of DNA polymerase in the RT assay. One would have been motivated to suppress the RT activity in order to obtain more accurate results with regard to the actual RT activity of the sample, not the DNA polymerase. One would have had a reasonable expectation of success that the addition of calf thymus DNA would have suppressed DNA polymerase activity in Arnold's method because Lugert's uses calf thymus DNA in similar RT-PCR method. Although Lugert does not disclose the exact ratios of calf thymus DNA to known RNA template, given the amounts that are provided (page 212, second and third columns), it would have been well within the ability of the ordinary artisan to optimize the amount of calf thymus DNA required to suppress the false positives given by RT activity of DNA polymerases. Therefore, the claimed embodiments would have been obvious to one of ordinary skill in the art at the time the invention was made.

12. Claims 1-16 and 18-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lovatt *et al.* (*Journal of Virological Methods*, October 1999, 82:185-200, "Lovatt") in view of . Burke (*Promega Notes Magazine*, 1996, Number 58, page 43, computer print-out is three pages). The Office recognizes that the instant application is entitled to the benefit of the filing date of foreign application 9923846.1, filed October 9, 1999. The examiner is investigating the public availability date of the Lovatt reference. Given that the Lovatt reference was in the October 1999 issue, it is expected that the public availability date of the October issue was prior to October 9, 1999, since many journals are mailed prior to the date on the cover. This has yet to be confirmed. If Applicant has any knowledge of the public availability date (day) of the Lovatt reference, Applicant is requested to be forthcoming with that information. If the date of availability was on or after October 9, 1999, any rejection based on the Lovatt reference will be withdrawn.

The Lovatt reference discloses the limitations of the instant invention represented in claims 1-16 and 18-30, with the exception of the treatment to substantially inactivate DNase present in the sample prior to PCR. However, Burke discloses that in instances where DNase is present in the sample (if the treatment is necessary prior to amplification), its removal can be performed by a phenol extraction and subsequent precipitation, or by heating at 95°C for 10 minutes (second page of computer print-out, first complete question/answer). One would have been motivated to use a DNase in order to purify the RNA sample as much as possible, and then inactivate the DNase prior to RT-PCR so that the results more accurately reflect the RT activity (Burke, first page of computer print-out, last question/answer). One would have had a reasonable expectation of success that further purification of the RNA in the sample would yield

more accurate results given that the DNA desired for amplification is the synthesized DNA and not DNA already present in the sample. Therefore, the claimed embodiments would have been obvious to one of ordinary skill in the art at the time the invention was made.

13. Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lovatt *et al.* (*Journal of Virological Methods*, October 1999, 82:185-200, "Lovatt") in view of . Burke (*Promega Notes Magazine*, 1996, Number 58, page 43, computer print-out is three pages) and Palmiter *et al.* (U.S. Patent 5,583,009, "Palmiter"). The claims are summarized above, as are the teachings of Lovatt and Burke. Neither Lovatt nor Burke disclose the use of a proteinase to inactivate DNase.

However, Burke discloses that in instances where DNase is present in the sample (if the treatment is necessary prior to amplification), its removal can be performed by a phenol extraction and subsequent precipitation, or by heating at 95°C for 10 minutes (second page of computer print-out, first complete question/answer). Although Burke does not teach the use of a proteinase to remove the DNase, it would have been obvious to use a proteinase, such as proteinase K. Palmiter discloses the use of proteinase K in an RT-PCR method following treatment of total nucleic acid with DNase (col. 15, second paragraph of Example 6).

One would have been motivated to use a DNase in order to purify the RNA sample as much as possible, and then inactivate the DNase prior to RT-PCR so that the results more accurately reflect the RT activity (Burke, first page of computer print-out, last question/answer). One would have had a reasonable expectation of success that further purification of the RNA in the sample would yield more accurate results given that the DNA desired for amplification is the

synthesized DNA and not DNA already present in the sample. Therefore, the claimed embodiments would have been obvious to one of ordinary skill in the art at the time the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

15. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 5/17/07
STACY B. CHEN
PRIMARY EXAMINER